HealthPartners Institute Neuroscience Research

A clinical trial for treatment of Traumatic Brain Injury through patented use of intranasal insulin

Neurological diseases are rising rapidly

Thanks to medical advances and the widespread adoption of healthy lifestyles, we are living longer. Researchers are learning more about the brain. We believe we can now treat Parkinson's, Alzheimer's, Traumatic Brain Injury, Post Traumatic Stress Disorder, and other brain diseases and disorders. Our goal is to prove this and gain FDA approval for commercialization of our patented use of Intranasal Insulin.

To conduct the finest and most promising research toward a cure, we need your help in raising awareness and identifying philanthropic partners.

Innovation takes time and requires significant and sustained investment. Loyal and generous friends have been the engine supporting our groundbreaking discoveries for over 30 years.

Approval for use of intranasal insulin is the first step toward making it available for other neurological conditions. We hope you will consider partnering with us in our efforts to conduct a Phase 2 Trial and expedite the path to commercialization.

Thank you for your interest in this exciting and important work.

Approximate number of people affected:
5M Alzheimer's Disease
2M Other dementias
2M Traumatic brain injuries
1M Parkinson's Disease

Source: https://dio.org/10.1002/ana.24897

Our discoveries

In 1989, William H. Frey II, PhD, discovered that natural therapeutics could be delivered directly from the nose to the brain along the nerves involved in smell. Dr. Frey's noninvasive intranasal delivery method was the first to bypass the blood-brain barrier to target therapeutic agents to the brain while reducing systemic exposure and unwanted side effects. The delivery method has captured the interest of both pharmaceutical companies and scientists worldwide.

We are now using this intranasal delivery method to administer and test exciting medications such as insulin for treating traumatic brain injury and post-traumatic stress disorder. In addition, intranasal insulin has shown promise as a treatment for Alzheimer's, Parkinson's and Lewy Body Dementia.

We are confident that once we gain FDA approval and commercialization for intranasal insulin to treat TBI, the waterfall of treatment possibilities will follow including use in patients with Alzheimer's and Parkinson's disease and other neurological disorders.

Philanthropy has allowed HealthPartners Institute to make important breakthroughs in neuroscience research

We currently have 46 active studies involving neurological disorders.
In addition, we collaborate with more than a dozen researchers worldwide who are using the intranasal delivery method in their own research.

"These neurodegenerative diseases are not incurable — researchers around the world are following our lead to find cures."

William H. Frey II, PhD

Meet our neuroscience research leaders

William H. Frey II, PhD, is co-director of neuroscience research at HealthPartners Neuroscience Center in St. Paul, Minnesota. Dr. Frey earned his BA in chemistry at Washington University and PhD in biochemistry at Case Western Reserve University. His patents, owned by HealthPartners Institute, Novartis, Stanford University and others, target the delivery of insulin and other therapeutic agents to the brain for treating neurological and psychiatric disorders. With over 100 publications in scientific and medical journals, Dr. Frey has been interviewed on Good Morning America, The Today Show, 20/20, and All Things Considered. Articles about Dr. Frey's research have appeared in the Wall Street Journal, The New York Times and other magazines and newspapers around the world.

Leah Hanson, PhD is co-director of neuroscience research at HealthPartners Neuroscience Center in St. Paul, Minnesota. Dr. Hanson received her BS in biology from Drake University in Des Moines, Iowa and her PhD in neuroscience from the University of Minnesota, Twin Cities. Her research interests include the prevention and treatment of Alzheimer's disease and other neurodegenerative disorders, including the development of drugs that are intranasally administered to target the brain and treat neurodegenerative disorders. In addition, she focuses her research on how lifestyle changes, including exercising the body and mind, can prevent memory loss associated with aging.

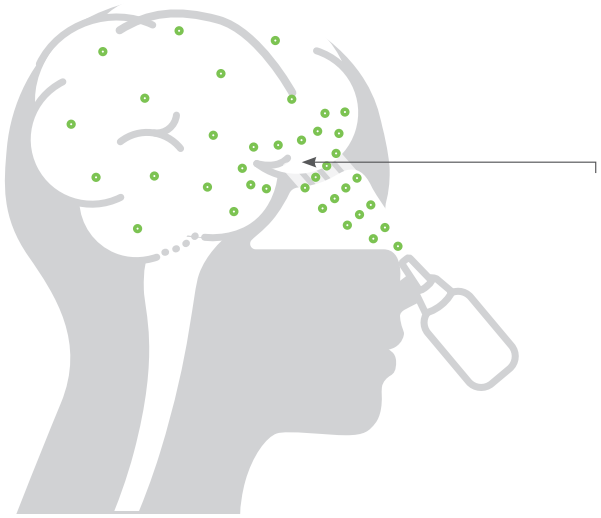
Intranasal insulin as treatment for traumatic brain injury

In multiple clinical trials in patients with Alzheimer's disease and healthy adults, intranasal insulin safely improves memory and metabolism, increases brain cell energy and reduces white matter damage. Preclinical studies demonstrate that following traumatic brain injury (TBI) intranasal insulin improves memory, increases cerebral glucose uptake, decreases neuroinflammation and brain damage and therefore looks promising as a treatment for TBI.

The Promise of Intranasal Delivery:

- Direct nose-to-brain delivery
- Bypasses the blood-brain barrier
- Targets the brain: reduces systemic exposure increasing risks to other organs
- Rapid: uptake may be measurably observed in under 10 minutes
- Non-invasive: applied using a nasal spray device

Insulin is a generic drug, providing an expedited path to commercialization. Our goal is to complete a Phase 2 clinical trial for TBI. Upon completion, we will sell licensing rights to our patent so Phase 3 clinical trials can be administered.



Intranasal delivery
Medicine delivered along the nerves in the nasal passage bypasses the blood-brain barrier and enters the brain directly.

Diagram for illustrative purposes only.

Path to commercialization

Phase 2 clinical trial testing the efficacy of intranasal insulin in patients with TBI and head injury

History: completed intranasal insulin research

- Safety and efficacy in healthy adults with improved memory and increased brain cell energy
- Improved memory and reduced white matter degeneration in clinical trials in patients with Mild Cognitive Impairment (MCI) or Alzheimer's
- Alzheimer's studies overall demonstrate benefit, especially as various insulin types are selected based on the patient's genetics
- Evidence in animals with moderate TBI of improved memory and increased cerebral glucose uptake with decreased neuroinflammation and hippocampal lesion volume

In process with plans to complete by end of 2024

- Testing of devices for intranasal insulin treatment
- The US Department of Defense has contributed $1.5 million through the US Military School and HealthPartners Neuroscience Center to conduct an IN study for TBI in a mouse, rat and ferret study. Currently we are administering another study with mice and rats.
- Phase 1a in 12 healthy adults to validate drug/device combination and demonstrate intranasal insulin reaches cerebrospinal fluid
- Develop a proposal to the FDA for approval of a Phase 2 clinical trial for patients with a TBI, including full budget and timeline

Next steps, current need and high priority funding

- Secure philanthropy to fund the Phase 2 trial
- Submit proposal to the FDA including established protocol
- Facilitate and complete trial to generate FDA approval

Once Phase 2 is complete, we plan to license our patent to a partner who can administer Phase 3 **and bring it to commercialization.**

Philanthropic investment:

$100,000 investment fully funded for Phase 2 trial planning (gain initial approvals, develop a full budget, timeline, and submit all of the necessary documentation for FDA trial approval.)

$2Mfor Phase 2 trial to commence as soon as funding is secured.

HealthPartners Institute clinical trial expertise

At HealthPartners Institute, there are at least 100 active clinical trials at any point in time.

With 1.2 million patients and 2 million insurance members, we have the opportunity to identify potentially eligible patients.

We have a sophisticated clinical trial management system and project coordination expertise, with support from operations for clinical trials are research.

Often, our clinical trials provide hope for patients and families.

HealthPartners Institute neuroscience research

Why we are best suited to tackle and treat neurological diseases:

- ✓ We are the only non-profit research institution that has successfully developed a treatment that safely improves memory, attention and functioning in patients with Alzheimer's.
- ✓ We are also the only healthcare organization offering extensive clinical trials for patients with dementia using treatments discovered in its own labs.
- ✓ We are conducting the complete range of neurological research, from the studies needed before human trials can begin, to human trials, to research using electronic medical records to track the progress of patient populations over time.
- ✓ Philanthropic investments of over $13 million enabled us to move our neurosciences research labs from Regions Hospital and create HealthPartners Neuroscience Center, outfitted with state-of-the-art equipment to more than double the research potential and, crucially, design and execute human clinical trials.
- ✓ Protected Physician Time; our physicians and researchers collaborate to develop our research platform. Protected time for physicians allows them to partner with our scientists in research that addresses challenges encountered by their patients.
- ✓ This patient-centered research results in papers published for the benefit of clinicians around the world and spurs changes in clinical practice.
- ✓ With research and outpatient care operating under the same roof, multidisciplinary teams collaborate during patient care and quickly identify patients who are eligible for participation in clinical trials.
- ✓ The research team currently is comprised of 16 staff, including 5 PhD investigators, 2 research coordinators, 3 research assistants, a biostatistician as well as support staff.

Applying intranasal insulin to other disorders

Once clinical trials are complete, intranasal insulin treatment of TBI can advance development of intranasal insulin for Post Traumatic Stress Disorder (PTSD) and other disorders and diseases.

Completed trials will indirectly advance the intranasal treatment of Alzheimer's, Parkinson's, Anorexia, and Social Communication Disorder.

Note: new drugs under development to reduce insulin resistance will likely increase the efficacy of intranasal insulin treatment of Alzheimer's and other brain disorders.

> “Intranasal delivery of medications to the brain is one of the most innovative and promising areas of research that may provide improved brain function and recovery in a several different brain diseases. This area of research was invented right here at Regions Hospital and continues to be one of the most exciting areas of research in brain diseases.”
>
> Bret Haake, MD, Neurology,
> VP Medical Affairs, CMO Regions Hospital

HealthPartners Institute is part of HealthPartners, the largest consumer governed nonprofit health care organization in the nation with a mission to improve health and well-being in partnership with our members, patients, and the community.

HealthPartners Institute supports this mission through research and education—advancing care delivery and public health around the globe. The Institute annually conducts more than 350 research studies and trains 700+ medical residents and fellows and 1,200+ medical and advanced practice students.

Its integration with HealthPartners' hospitals, clinics and health plan strengthens the Institute's ability to discover and develop evidence-based solutions and translate them into practice. Visit healthpartnersinstitute.org for more information.

HealthPartners Institute

Shelly Rucks
Senior Development Officer
Cell: **(612)-816-1139**
shelly.r.rucks@healthpartners.com

RHF
Mail Stop 11202C
640 Jackson Street
St. Paul, MN 55101-2595